

What is claimed:

1. A method of diagnosing a thyroid condition in a subject which comprises:
- 5 a) obtaining a suitable urine sample from the subject;
- 10 b) determining the concentration of thyroid stimulating hormone in the sample by a method which is not a radioimmunoassay; and
- 15 c) comparing the concentration of thyroid stimulating hormone with a urinary concentration of thyroid stimulating hormone in a normal subject;
- wherein:
- 20 i) a concentration of thyroid stimulating hormone which is higher than the urinary concentration of thyroid stimulating hormone in the normal subject diagnoses hypothyroidism in the subject; and
- 25 ii) a concentration of thyroid stimulating hormone which is lower than the urinary concentration of thyroid stimulating hormone in the normal subject diagnoses hyperthyroidism in the subject.
- 30 2. The method of claim 1, wherein step (b) comprises:
- 35 (1) contacting an agent capable of binding to thyroid stimulating hormone with the urine sample so as to bind thyroid stimulating hormone which is present in the sample to the agent;

- (2) removing unbound urine sample;
- (3) contacting the bound thyroid stimulating hormone with a detectable agent capable of binding to thyroid stimulating hormone so as to bind the detectable agent to the bound thyroid stimulating hormone;
- (4) removing unbound detectable agent; and
- (5) determining the amount of detectable agent which is bound to the thyroid stimulating hormone, thereby determining the amount of thyroid stimulating hormone in the urine sample.
3. The method of claim 2, wherein the agent capable of binding to thyroid stimulating hormone of step (1) is an antibody which binds to thyroid stimulating hormone.
4. The method of claim 2, wherein the agent capable of binding to thyroid stimulating hormone of step (1) is a thyroid stimulating hormone receptor.
5. The method of claim 2, wherein the detectable agent is an antibody which binds to an epitope on thyroid stimulating hormone which differs from the epitope to which the agent of step (1) binds.
6. The method of claim 2, wherein the detectable agent is labeled with a detectable marker.
7. The method of claim 1, wherein a concentration greater than 0.35 μ IU/ml diagnoses hypothyroidism in the subject.

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(1) contacting an agent capable of binding to

triiodothyronine with a pre-determined amount

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14. The method of claim 10 or 11, wherein the detectable triiodothyronine is labeled with a detectable marker.
- 5 15. The method of claim 9, wherein a concentration less than 0.3 ng/ml diagnoses hypothyroidism in the subject.
- 10 16. The method of claim 9, wherein a concentration greater than 1.5 ng/ml diagnoses hyperthyroidism in the subject.
17. A method of diagnosing a thyroid condition in a subject which comprises:
- 15 a) obtaining a suitable urine sample from the subject;
- b) determining the concentration of triiodothyronine- sulfate in the sample by a method which is not a radioimmunoassay;
- 20 and
- c) comparing the concentration of triiodothyronine- sulfate with a urinary concentration of triiodothyronine-sulfate in a normal subject;
- 25 wherein
- i) a concentration of triiodothyronine-sulfate which is lower than the urinary concentration of triiodothyronine-sulfate in the normal subject diagnoses hypothyroidism in the subject; and
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- 35 ii) a concentration of triiodothyronine-

5 sulfate which is higher than the
urinary concentration of
triiodothyronine-sulfate in the
normal subject diagnoses
hyperthyroidism in the subject.

18. The method of claim 17, wherein step (b) comprises:

- 10 (1) contacting an agent capable of binding to
triiodothyronine-sulfate with a pre-determined
amount of detectable triiodothyronine-sulfate
and the urine sample, so as to form a complex
between the agent and (i) the detectable
triiodothyronine-sulfate or (ii) the
15 triiodothyronine-sulfate present in the urine
sample;
- (2) determining the amount of detectable
triiodothyronine-sulfate which is bound to the
agent, wherein the difference between the pre-
determined amount of detectable
20 triiodothyronine-sulfate and the amount of
detectable triiodothyronine-sulfate which is
bound indicates the amount of triiodothyronine-
sulfate present in the urine sample.

25 19. The method of claim 18, wherein step (b) comprises:

- (1) contacting an agent capable of binding to
triiodothyronine-sulfate with a pre-determined
amount of detectable triiodothyronine-sulfate
and the urine sample, so as to form a complex
30 between the agent and (i) the detectable
triiodothyronine-sulfate or (ii) the
triiodothyronine-sulfate present in the urine
sample;
- (2) determining the amount of detectable
35 triiodothyronine-sulfate which is not bound to

the agent, thereby determining the amount of triiodothyronine-sulfate present in the urine sample.

- 5 20. The method of claim 18 or 19, wherein the agent of
step (1) which is capable of binding to
triiodothyronine-sulfate is an antibody.
- 10 21. The method of claim 18 or 19, wherein the agent of
step (1) which is capable of binding to
triiodothyronine-sulfate is a triiodothyronine
receptor.
- 15 22. The method of claim 18 or 19, wherein the detectable
triiodothyronine-sulfate is labeled with a
detectable marker.
- 20 23. The method of claim 17, wherein a concentration
lower than 0.1 ng/ml diagnoses hypothyroidism in the
subject.
- 25 24. The method of claim 17, wherein a concentration
higher than 0.5 ng/ml diagnoses hyperthyroidism in
the subject.
- 30 25. A method of diagnosing a thyroid condition in a
subject which comprises:
a) obtaining a suitable urine sample from the
subject;
- 35 b) determining the concentration of thyroxine
present in the sample by a method which is
not a radioimmunoassay;
- c) comparing the concentration of thyroxine

with a urinary concentration of thyroxine
in a normal subject;

wherein

i) a concentration of thyroxine which
is lower than the concentration of
thyroxine in the normal subject
diagnoses hypothyroidism in the
subject; and

ii) a concentration of thyroxine which
is higher than the urinary
concentration of thyroxine in the
normal subject diagnoses
hyperthyroidism in the subject.

26. The method of claim 25, wherein step (b) comprises:

(1) contacting an agent capable of binding to
thyroxine with a pre-determined amount of
detectable thyroxine and the urine sample, so
as to form a complex between the agent and (i)
the detectable thyroxine or (ii) the thyroxine
present in the urine sample;

(2) determining the amount of detectable thyroxine
which is bound to the agent, wherein the
difference between the pre-determined amount of
detectable thyroxine and the amount of
detectable thyroxine which is bound indicates
the amount of thyroxine present in the urine
sample.

27. The method of claim 25, wherein step (b) comprises:

(1) contacting an agent capable of binding to
thyroxine with a pre-determined amount of
detectable thyroxine and the urine sample, so
as to form a complex between the agent and (i)

the detectable thyroxine or (ii) the thyroxine present in the urine sample;

- (2) determining the amount of detectable thyroxine which is not bound to the agent, thereby determining the amount of thyroxine present in the urine sample.

28. The method of claim 26 or 27, wherein the agent of step (1) which is capable of binding to thyroxine is an antibody.

29. The method of claim 26 or 27, wherein the agent of step (1) which is capable of binding to thyroxine is a thyroxine receptor.

30. The method of claim 26 or 27, wherein the detectable thyroxine is labeled with a detectable marker.

31. The method of claim 25, wherein a concentration lower than 0.3 ng/ml diagnoses hypothyroidism in the subject.

32. The method of claim 25, wherein a concentration higher than 1.5 ng/ml diagnoses hyperthyroidism in the subject.

33. A method of diagnosing a thyroid condition in a subject which comprises:

a) obtaining a suitable urine sample from the subject;

b) determining the concentration of thyroxine-glucuronide present in the sample by a method which is not a radioimmunoassay;

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35. The method of claim 33, wherein step (b) comprises:
- 5 (1) contacting an agent capable of binding to thyroxine-glucuronide with a pre-determined amount of detectable thyroxine-glucuronide and the urine sample, so as to form a complex between the agent and (i) the detectable thyroxine-glucuronide or (ii) the thyroxine-glucuronide present in the urine sample;
- 10 (2) determining the amount of detectable thyroxine-glucuronide which is not bound to the agent, thereby determining the amount of thyroxine-glucuronide present in the urine sample.
- 15 36. The method of claim 34 or 35, wherein the agent of step (1) which is capable of binding to thyroxine-glucuronide is an antibody.
- 20 37. The method of claim 34 or 35, wherein the agent of step (1) which is capable of binding to thyroxine-glucuronide is a thyroxine receptor.
- 25 38. The method of claim 34 or 35, wherein the detectable thyroxine-glucuronide is labeled with a detectable marker.
- 30 39. The method of claim 33, wherein a concentration lower than 0.1 ng/ml diagnoses hypothyroidism in the subject.
40. The method of claim 33, wherein a concentration higher than 0.5 ng/ml diagnoses hyperthyroidism in the subject.
- 35 41. A method of diagnosing a thyroid condition in a subject which comprises:

- (2) obtaining a suitable urine sample from the subject;
- 5 b) determining the concentration of thyroid stimulating hormone and the concentration of triiodothyronine in the sample by a method which is not a radioimmunoassay;
- 10 c) comparing the concentration of thyroid stimulating hormone with a urinary concentration of thyroid stimulating hormone in a normal subject and comparing the concentration of triiodothyronine with a urinary concentration of triiodothyronine in a normal subject;
- 15 wherein
- 20 i) a concentration of thyroid stimulating hormone which is higher than the urinary concentration of thyroid stimulating hormone in the normal subject, and a concentration of triiodothyronine which is lower than the urinary concentration of triiodothyronine in the normal subject, diagnoses hypothyroidism in the subject; and
- 25 ii) a concentration of thyroid stimulating hormone which is lower than the urinary concentration of thyroid stimulating hormone present in the normal subject, and a concentration of triiodothyronine which is higher than the urinary concentration of triiodothyronine in
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the normal subject, diagnoses hyperthyroidism in the subject.

- 5 42. The method of ~~claim 41~~, wherein step (b) comprises:
- 10 (1) contacting an agent capable of binding to thyroid stimulating hormone with the urine sample so as to bind thyroid stimulating hormone which is present in the sample to the agent;
- (2) removing unbound urine sample;
- (3) contacting the bound thyroid stimulating hormone with a detectable agent capable of binding to thyroid stimulating hormone so as to
- 15 bind the detectable agent to the bound thyroid stimulating hormone;
- (4) removing unbound detectable agent; and
- (5) determining the amount of detectable agent which is bound to the thyroid stimulating hormone, thereby determining the amount of
- 20 thyroid stimulating hormone in the urine sample.
- 25 43. The method of ~~claim 42~~, wherein the agent capable of binding to thyroid stimulating hormone of step (1) is an antibody which binds to thyroid stimulating hormone.
- 30 44. The method of ~~claim 42~~, wherein the agent capable of binding to thyroid stimulating hormone of step (1) is a receptor which binds to thyroid stimulating hormone.
- 35 45. The method of ~~claim 42~~, wherein the detectable agent is an antibody which binds to an epitope on thyroid

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triiodothyronine present in the urine sample.

49. The method of claim 47 or 48, wherein the agent
capable of binding to triiodothyronine of step (1)
is an antibody which is capable of binding to
triiodothyronine.
50. The method of claim 47 or 48, wherein the agent
capable of binding to triiodothyronine of step (1)
is a triiodothyronine receptor.
51. The method of claim 47 or 48, wherein the detectable
triiodothyronine is labeled with a detectable
marker.
52. The method of claim 41, wherein a concentration of
thyroid stimulating hormone greater than 0.35 μ IU/ml
and a concentration of triiodothyronine greater
than 1.5 ng/ml diagnoses hypothyroidism in the
subject.
53. The method of claim 41, wherein a concentration of
thyroid stimulating hormone less than 0.04 μ IU/ml
and a concentration of triiodothyronine less than
0.3 ng/ml diagnoses hyperthyroidism in the subject.
54. A method of diagnosing a thyroid condition in a
subject which comprises:
- a) obtaining a suitable urine sample from the
subject;
 - b) determining the concentration of thyroid
stimulating hormone and the concentration
of thyroxine in the sample by a method
which is not a radioimmunoassay;

c) comparing the concentration of thyroid stimulating hormone with a urinary concentration of thyroid stimulating hormone in a normal subject and comparing the concentration of thyroxine with a urinary concentration of thyroxine in a normal subject;
wherein

i) a concentration of thyroid stimulating hormone which is higher than the urinary concentration of thyroid stimulating hormone in a normal subject, and a concentration of thyroxine which is lower than the urinary concentration of thyroxine in a normal subject, diagnoses hypothyroidism in the subject; and

ii) a concentration of thyroid stimulating hormone which is lower than the urinary concentration of thyroid stimulating hormone in a normal subject, and a concentration of thyroxine which is higher than the urinary concentration of thyroxine in a normal subject, diagnoses hyperthyroidism in the subject.

55. The method of claim 53, wherein step (b) comprises:

(1) contacting an agent capable of binding to thyroid stimulating hormone with the urine sample so as to bind thyroid stimulating hormone which is present in the sample to the

agent;

(2) removing unbound urine sample;

(3) contacting the bound thyroid stimulating hormone with a detectable agent capable of binding to thyroid stimulating hormone so as to bind the detectable agent to the bound thyroid stimulating hormone;

(4) removing unbound detectable agent; and

(5) determining the amount of detectable agent which is bound to the thyroid stimulating hormone, thereby determining the amount of thyroid stimulating hormone in the urine sample.

56. The method of claim 55, wherein the agent capable of binding to thyroid stimulating hormone of step (1) is an antibody which binds to thyroid stimulating hormone.

57. The method of claim 55, wherein the detectable agent is an antibody which binds to an epitope on thyroid stimulating hormone which differs from the epitope to which the agent of step (1) binds.

58. The method of claim 55, wherein the agent capable of binding to thyroid stimulating hormone of step (1) is a receptor which binds to thyroid stimulating hormone.

59. The method of claim 55, wherein the detectable agent is labeled with a detectable marker.

60. The method of claim 54, wherein step (b) comprises:

(1) contacting an agent capable of binding to thyroxine with a pre-determined amount of

detectable thyroxine and the urine sample, so as to form a complex between the agent and (i) the detectable thyroxine or (ii) the thyroxine present in the urine sample;

- 5 (2) determining the amount of detectable thyroxine which is bound to the agent, wherein the difference between the pre-determined amount of detectable thyroxine and the amount of detectable thyroxine which is bound indicates the amount of thyroxine present in the urine sample.
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61. The method of claim 54, wherein step (b) comprises:

- 15 (1) contacting an agent capable of binding to thyroxine with a pre-determined amount of detectable thyroxine and the urine sample, so as to form a complex between the agent and (i) the detectable thyroxine or (ii) the thyroxine present in the urine sample;
- 20 (2) determining the amount of detectable thyroxine which is not bound to the agent, thereby determining the amount of thyroxine present in the urine sample.

25 62. The method of claim 60 or 61, wherein the agent of step (1) which is capable of binding to thyroxine is an antibody.

30 63. The method of claim 60 or 61, wherein the agent of step (1) which is capable of binding to thyroxine is a thyroxine receptor.

35 64. The method of claim 60 or 61, wherein the detectable thyroxine is labeled with a detectable marker.

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68. The method of ~~claim 67~~, wherein step (b) comprises:

- (1) contacting an agent capable of binding to thyroid stimulating hormone with the urine sample so as to bind thyroid stimulating hormone which is present in the sample to the agent;
- (2) removing unbound urine sample;
- (3) contacting the bound thyroid stimulating hormone with a detectable agent capable of binding to thyroid stimulating hormone so as to bind the detectable agent to the bound thyroid stimulating hormone;
- (4) removing unbound detectable agent; and
- (5) determining the amount of detectable agent which is bound to the thyroid stimulating hormone, thereby determining the amount of thyroid stimulating hormone in the urine sample.

69. The method of ~~claim 68~~, wherein the agent of step (1) is an antibody which binds to thyroid stimulating hormone.

70. The method of ~~claim 68~~, wherein the detectable agent is an antibody which binds to an epitope on thyroid stimulating hormone which differs from the epitope to which the agent of step (1) binds.

71. The method of ~~claim 68~~, wherein the agent of step (1) which is capable of binding to thyroxine is a thyroid stimulating hormone receptor.

72. The method of ~~claim 68~~, wherein the detectable agent is labeled with a detectable marker.

73. The method of claim 67, wherein a concentration higher than 0.35 μ IU/ml or a concentration lower than 0.04 μ IU/ml indicates that the subject is not receiving the proper dosage of thyroxine.

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74. A method of determining whether a subject being treated with thyroxine is receiving a proper dosage of thyroxine which comprises:

10 a) obtaining a suitable urine sample from the subject;

15 b) determining the concentration of triiodothyronine in the sample by a method which is not a radioimmunoassay; and

20 c) comparing the concentration of triiodothyronine with a urinary concentration of triiodothyronine in a normal subject;

25 wherein a concentration of triiodothyronine which is higher or lower than the urinary concentration of triiodothyronine in a normal subject indicates that the subject is not receiving the proper dosage of thyroxine.

75. The method of claim 74, wherein step (b) comprises:

30 (1) contacting an agent capable of binding to triiodothyronine with a pre-determined amount of detectable triiodothyronine and the urine sample, so as to form a complex between the agent and (i) the detectable triiodothyronine
35 or (ii) the triiodothyronine present in the

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urine sample; and

- (2) determining the amount of detectable triiodothyronine which is bound to the agent, wherein the difference between the pre-determined amount of detectable triiodothyronine and the amount of detectable triiodothyronine which is bound indicates the amount of triiodothyronine present in the urine sample.

76. The method of ~~claim 74~~, wherein step (b) comprises:

- (1) contacting an agent capable of binding to triiodothyronine with a pre-determined amount of detectable triiodothyronine and the urine sample, so as to form a complex between the agent and (i) the detectable triiodothyronine or (ii) the triiodothyronine present in the urine sample;

- (2) determining the amount of detectable triiodothyronine which is not bound to the agent, thereby determining the amount of triiodothyronine present in the urine sample.

77. The method of ~~claim 75 or 76~~, wherein the agent of step (1) which is capable of binding to triiodothyronine is an antibody.

78. The method of ~~claim 75 or 76~~, wherein the agent of step (1) which is capable of binding to triiodothyronine is a triiodothyronine receptor.

79. The method of ~~claim 75 or 76~~, wherein the detectable triiodothyronine is labeled with a detectable marker.

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(2) determining the amount of detectable thyroxine which is bound to the agent, wherein the

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88. A method of monitoring a subject being treated with thyroxine and ensuring that the subject receives the proper dosage of thyroxine which comprises:

- (a) determining whether the subject is receiving the proper dosage of thyroxine the method of any one of claims 67, 74 and 81;
- (b) adjusting the dosage if it is determined that the subject is not receiving the proper dosage;
- (c) repeating steps (a) through (b) throughout the course of the treatment;

thereby monitoring the subject being treated with thyroxine and ensuring that the subject receives the proper dosage of thyroxine.

- 15 89. The method of any one of claims 2, 10, 11, 18, 19,
26, 27, 34, 35, 42, 43, 47, 48, ~~55,~~ 60, 61, 68, 75,
76, 82 and 83, wherein the agent of step (1) is
immobilized.

- 20 90. The method of claim 89, wherein the agent is immobilized on a gold particle, a latex particle, a magnetic particle or other solid phase.

91. The method of any one of claims ~~1, 9, 17, 25, 33,~~
41, 54, 67, 74 and 81, wherein the urine sample is
concentrated.

92. The method of any one of claims ~~1, 9, 17, 25, 33,~~
41, 54, 67, 74 and 81, wherein the urine sample is
not concentrated.

93. The method of any one of claims 6, 14, 22, 30, 38, 46, 51, 59, 64, 72, 79 and 86, wherein the detectable marker is a colorimetric, a luminescent, or a fluorescent marker.